Integrating buprenorphine maintenance therapy into federally qualified health centers: Real-world substance abuse treatment outcomes

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ABSTRACT

Background: Few studies have examined real-world effectiveness of integrated buprenorphine maintenance treatment (BMT) programs in federally qualified health centers (FQHCs).

Methods: Opioid dependent patients ($N = 266$) inducted on buprenorphine between July 2007 and December 2008 were retrospectively assessed at Connecticut's largest FQHC network. Six-month BMT retention and opioid-free time were collected longitudinally from electronic health records; 136 (51.1%) of patients were followed for at least 12 months.

Results: Participants had a mean age of 40.1 years, were primarily male (69.2%) and treated by family practitioners (70.3%). Co-morbidity included HCV infection (59.8%), mood disorders (71.8%) and concomitant cocaine use (59%). Retention on BMT was 56.8% at 6 months and 61.6% at 12 months for the subset observed over 1 year. Not being retained on BMT at 12 months was associated with cocaine use (AOR = 2.18; 95% CI = 1.35–3.50) while prescription of psychiatric medication (AOR = 0.36; 95% CI 0.20–0.62) and receiving on-site substance abuse counseling (AOR = 0.34; 95% CI 0.19, 0.59) improved retention. Two thirds of the participants experienced at least one BMT gap of 2 or more weeks with a mean gap length of 116.4 days.

Conclusions: Integrating BMT in this large FQHC network resulted in retention rates similarly reported in clinical trials and emphasizes the need for providing substance abuse counseling and screening for and treating psychiatric comorbidity.

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1. Background

Opioid dependence and abuse, including use of heroin or prescription pain killers, affects approximately 2.28 million Americans (SAMHSA, 2011). Opioid substitution therapy, such as methadone and buprenorphine, has documented effectiveness in treating opioid dependence (Connock et al., 2007; Mattick et al., 2008). Access to specially licensed and highly structured methadone maintenance programs, however, is limited, leaving 80–85% of the opioid-dependent population untreated (Friedman et al., 2007). The Drug Addiction Treatment Act of 2000 and the approval of buprenorphine in 2002 allowed certified physicians to prescribe buprenorphine in primary and specialty care settings, making opioid maintenance treatment more available and easier to access (Altice et al., 2006; Basu et al., 2006).

In March 2010, the U.S. Congress passed the Affordable Care Act (ACA) to substantially reduce the number of uninsured Americans and the United States Supreme Court largely upheld the healthcare reform law in June 2012. The ACA seeks to increase access to affordable, high quality healthcare and thus supports expanded healthcare delivery in federally qualified health centers (FQHCs). FQHCs are public or private non-profit health centers governed by a community board that are grant-supported under the Public Health Service Act and provide comprehensive primary care services in communities where there is a need to provide care for the medically underserved. Those individuals who have lower education, are unemployed, live in metropolitan areas or who are on probation or parole have higher rates of substance dependence or abuse (SAMHSA, 2011) and many FQHCs serving these individuals strive to deliver comprehensive and integrated healthcare including mental health services. Nevertheless, despite the capability of primary care physicians (PCPs) to prescribe buprenorphine, barriers persist that prevent expansion of buprenorphine maintenance treatment (BMT; Barry et al., 2009; Netherland et al., 2009).

Aside from efficacy trials conducted in primary care settings, few studies examine the relative effectiveness of BMT that is provided in

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real-world FQHC. Most studies examining BMT in primary care centers are either university-affiliated or hospital-based (Alford et al., 2011; Altice et al., 2011; Fiellin et al., 2008; Harris et al., 2005; Mintzer et al., 2007; Soeffing et al., 2009; Stein et al., 2005). Thus, real-world clinical effectiveness studies are likely helpful to support further expansion of BMT. Provision of BMT in FQHCs, which cater to medically underserved populations, is even more critical since vulnerable patients from these centers urgently need opioid substitution therapy.

Patients with opioid dependence often have multiple medical and psychiatric co-morbidities (Altice et al., 2010). Therefore, integrating BMT in healthcare settings allows for the simultaneous treatment of multiple comorbidities (Altice et al., 2010; Korthuis et al., 2011; Sylla et al., 2007). There are currently few clinical effectiveness studies conducted in FQHCs that examine the factors related to buprenorphine's effectiveness in treating opioid dependence and simultaneously engaging them in routine primary care, including prevention, diagnosis, and treatment of co-morbid medical conditions (e.g. HIV, HCV, HBV, hyperlipidemia, and hypertension). In this paper, we examine real-world substance abuse treatment outcomes in patients within a FQHC network. Such findings have important implications for other countries globally where BMT can be prescribed in primary care settings and reassure countries where BMT remains highly regulated.

2. Methods

2.1. Source of study population

Community Health Center, Inc. (CHC) is Connecticut's largest FQHC network, comprised of 13 sites. Two of the largest sites are located in the impoverished cities of New Britain and Meriden and serve over 28,500 patients of whom the majority are people of color [Hispanics (56%), Blacks (10%)] and are on Medicaid (71%), while 17% are uninsured. During the study period, four physicians were certified and providing BMT at these two sites; three were family physicians and one was a psychiatrist.

2.2. Description of the buprenorphine maintenance treatment program

BMT began at CHC in 2006 with one psychiatrist prescribing in New Britain and Meriden. By 2007, two family practitioners in Meriden and one in New Britain initiated BMT resulting in a standardized induction and stabilization protocol based on SAMHSA's Treatment Improvement Protocol 40 (Center for Substance Abuse Treatment, 2004). Induction was primarily observed within the clinic; however, occasionally home induction occurred (Gunderson et al., 2010). Patients were generally reassessed weekly over the first 2 weeks. Thereafter, patients were usually seen every 1–4 weeks, depending on provider determination. Urine toxicology screens were typically collected at every visit. Supervised urine collection and buprenorphine pill counts were done at the discretion of the provider. Patients were initially referred to either on- or off-site substance abuse counseling, depending on provider preference and availability. Management of urine test results positive for illicit drugs, including heroin and cocaine, remained at the discretion of the individual provider. For patients deemed not succeeding on BMT, referral to off-site intensive outpatient counseling, inpatient treatment, methadone maintenance, or discharge from the program would usually result. Buprenorphine prescriptions were sent to two designated pharmacies that dispensed the medication only upon the patient's presentation of a validated voucher embossed by an authorized healthcare provider. The CHC protocol served only as a guide to providers and thus inter-provider variability in patient management existed based on differences in style and philosophy of practice.

2.3. Study design and sample

In this retrospective, observational study, persons were included in the cohort if they were ≥18 years, met DSM-IV criteria for opioid dependence, were prescribed at least one prescription for buprenorphine by a CHC provider between July 1, 2007 and December 1, 2008, and received treatment at either the New Britain or Meriden site. Overall, 266 patients met the inclusion criteria and were included in the analysis. Study participants were identified through the electronic health record (EHR) for anyone prescribed buprenorphine. The dates of enrollment were chosen since the BMT protocol had been adopted and the EHR had been fully implemented at all CHC health center sites by July 1, 2007.

All subjects were observed for at least 6 months beyond the date of their first prescription, with a range from 6 to 21.5 months. Observation consisted solely of review of the EHR. For this analysis, outcomes of interest were related to substance abuse treatment outcomes, including retention in care, treatment gaps, and opioid-free time.

2.4. Study procedure

A standardized data collection instrument was created for the electronic chart review. The instrument included age, healthcare site, type of buprenorphine prescriber (family practitioner or psychiatrist), all FQHC visits, buprenorphine prescription doses and dates, medication lists, problem lists, and laboratory results including urine toxicology screening tests. Two research assistants independently extracted these data and where there was data entry discordance, the lead author (MSH) resolved the discrepancy.

2.5. Measures

2.5.1. Covariate definitions. The main reason for entry into care at CHC was considered primary care if subjects were engaged at the FQHC for longer than a month prior to being evaluated for BMT. If BMT was requested at the first visit or within one month of enrolling at the FQHC, then BMT was considered their reason for entry.

Co-morbidity data were based on International Classification of Diseases, 9th Revision (ICD-9) coding in the EHR and included: HIV, HCV, and HBV infections; metabolic disorders, including diabetes, hypertension, hyperlipidemia, and coronary artery disease; pulmonary disorders including asthma and chronic obstructive pulmonary disorder; and mood disorders including depression, anxiety, bipolar and psychotic disorders. Subjects prescribed anti-depressant, anti-anxiety, anti-psychotic, and mood stabilizing medications, were also identified. Either the primary care or behavioral health provider could have prescribed these psychiatric medications.

Co-morbid cocaine use was defined in two ways: (1) positive upon entry if cocaine was detected at baseline or within 1 week after induction and (2) positive if detected in at least one urine sample any time during the observation period.

The number and type of visits to the FQHC were divided into (1) medical visits, which included visits to a medical provider, nurse, nutritionist, or podiatrist, (2) behavioral health visits, which included visits to a psychiatrist, behavioral health prescriber, or clinician, and (3) on-site substance abuse counseling visits, which included individual or group visits with the substance abuse counselor. A subject was considered to have received substance abuse counseling on-site if he or she attended one or more individual or group visits with the substance abuse counselor; these visits were documented in the EHR.

2.5.2. Substance abuse outcome definitions. The primary outcome was retention on buprenorphine. Retention on buprenorphine was defined as being on BMT at the end of a pre-specified time period, similar to other studies which defined retention as the time until initial discontinuation of BMT (Alford et al., 2011; Cunningham et al., 2008; Moore et al., 2007; Parran et al., 2010; Soeffing et al., 2009). Retention was assessed at 1, 3, 6, and 12 months. In recognition that opioid dependence is a chronic relapsing disease, subject data were not censored if they discontinued BMT and were later re-inducted.

In addition, subjects were examined for persistence on BMT, a concept that recognizes recurrent treatment episodes (Bae et al., 2011; Ing et al., 2011). Treatment persistence was defined as receiving buprenorphine prescriptions continuously without any gaps in treatment of 2 weeks or more. Non-persistent treatment was defined as experiencing one or more gaps of 2 weeks or more in buprenorphine prescriptions and it included the gap between the end of the last prescription given and the end of observation period. Indeed, patients who missed receiving a buprenorphine prescription for 2 weeks or more may have tapered their dose or obtained buprenorphine outside the health center until they returned to the clinic. Individual charts were not reviewed to see if buprenorphine was continued during their absence from the clinic. Given easy accessibility of appointments at the FQHC, however, choosing a buffer of 2 weeks was assumed to be adequate in limiting potential misclassifications of non-persistence treatment. This approach acknowledged the integrated chronic disease model of care espoused by FQHCs as it is applied to the chronic and relapsing nature of opioid dependence.

A secondary outcome was opioid-free time. This outcome was defined in three distinct ways because of the inconsistency reported in previous studies. The first two definitions, similar to those examined by others to allow for comparison with existing data, were (1) no urine opioids in the last month of observed treatment (Alford et al., 2011, 2007, 2004; Cunningham et al., 2011; Soeffing et al., 2009) and (2) the percentage of all collected opioid-free urines (Fiellin et al., 2008; Kakko et al., 2007, 2003; Moore et al., 2007; O'Connor et al., 1998). In an attempt to correct for the real-world discrepancy in the number of urines collected per person over the variable lengths of time each person was on treatment, we created a third definition, the duration of opioid-free time while on prescribed buprenorphine, by multiplying the percentage of all collected opioid-free urine samples by the length of time the patient was on BMT, but excluding the documented gaps in treatment. Urine screens included in the analysis started with the first urine collected one week after buprenorphine induction, which we defined as baseline.

2.6. Statistical analysis

To address the issue of missing data, a series of multiple imputations were performed using a *Markov Chain Monte Carlo* (MCMC) simulation, conditional on variables which were observed (Jackman, 2000). Urine testing data were missing for only 5% and 3% of subjects for opioids and cocaine, respectively. For subjects who had urines collected, 12% and 4% had missing data for opioids and cocaine in the last observation month, respectively. Using MCMC simulation, the propensity of missing urine test results was not statistically related to the number of opioid and cocaine screening tests. *Missing at Random* (MAR) assumption was therefore invoked, which specifies that the probability of missing values is related to other observed covariates, but not the values of the missing variable itself (Enders, 2010). Sensitivity analyses conducted using additional simulations, confirm that the results were not sensitive to the departures from the MAR assumption.

Average BMT retention was analyzed by estimating a series of Cox proportional hazard models, where the outcome was defined in terms of whether the subject was on or off BMT based on pharmacy refill data. Consistent with the chronic and relapsing nature of opioid dependence, subjects were not censored from subsequent time points if they experienced a treatment gap and were re-inducted. The covariates in the Cox regression model included age, gender, site, prescriber specialty, cocaine use (both as 'baseline urine positive' and as 'at least one urine positive anytime during observation'), receipt of on-site substance abuse counseling, receipt of psychiatric medication, and presence of co-morbid mood disorder, and HIV and HCV infections.

In univariate analyses, covariates found to be statistically significant at $P < 0.20$ were modeled to determine the subset of the covariates which accounted for most of the variation in the dependent variable and then included in the multivariate analysis. The Wald test was used to assess the significance of the coefficients.

We evaluated the variability in the opioid-free time using several distinct models based on the three definitions of opioid-free time and a set of covariates. Because the first definition of opioid-free time was based on a dichotomous measure assessing whether the urine sample was opioid-free in the last month of treatment, we used logistic regression. Because our second definition was based on a percent of opioid-free urine samples, we employed a generalized linear model with a logit link. Since our third definition was based on a continuous measure expressed in units of days, we used an ordinary least square regression, in which the standard errors were adjusted for heteroskedasticity. In all three cases, the covariates that were found to be significant at $P < 0.20$ were included into the multivariate framework. The final multivariate model estimated in all three cases was based on the Akaike Information Criterion (AIC). All statistical analyses were conducted using STATA v.11.1 (StatCorp, College Station, TX).

3. Results

3.1. Characteristics of the study population

Of the 266 eligible subjects, the mean age was 40.1 years and most were male (69.2%), prescribed buprenorphine by a family practitioner (70.3%) and had established care at the FQHC primarily seeking BMT (80.5%). Thus, most patients entered primary care in search of substance abuse treatment. Subjects had significant co-morbidity including HIV infection (10.9%), HCV infection (59.8%), and a mood disorder (71.8%) with 65.0% being prescribed psychiatric medications. Over a third had a metabolic disorder and 17.7% had a chronic pulmonary disorder (Table 1).

3.2. Healthcare utilization at the FQHC

Most (90.6%) patients attended at least one medical visit, averaging 1.7 medical visits per month of BMT. At least one behavioral health visit was utilized by 56.3% of subjects, averaging 1.6 visits per month while on BMT. Over half (53.0%) attended at least one on-site substance abuse counseling visit, averaging 1.2 sessions per month of treatment. Overall, subjects averaged 3.1 visits to the health center for any reason per month on BMT, ranging from 0.5 to 8.3 visits per month (Table 2).

3.3. Buprenorphine dosing

In this cohort, the mean daily buprenorphine dose was 15.4 mg, achieved 2–4 weeks post-induction, and 17.8 mg, based on the last prescription dispensed, with a range for both between 2 and 32 mg. Less than a fifth (17.7%) of subjects were prescribed a daily dose

Table 1

Baseline characteristics of 266 opioid dependent patients initiating buprenorphine treatment.

Patient characteristic	N (%)
Age, mean (range)	40.1 (20–64)
Gender	
Male	184 (69.2)
Female	82 (30.8)
Clinical site	
Site 1	157 (59.0)
Site 2	109 (41.0)
Specialty of buprenorphine prescriber	
Primary care	187 (70.3)
Psychiatry	79 (29.7)
Main reason for entry into federally qualified health center	
Buprenorphine maintenance treatment	214 (80.5)
Primary care treatment	52 (19.5)
Co-morbidities (based on ICD-9 coding in electronic medical record)	
HIV infection	29 (10.9)
HCV infection	159 (59.8)
HBV infection	3 (1.1)
Metabolic disorder (diabetes, hypertension, hyperlipidemia, coronary artery disease)	94 (35.3)
Pulmonary disorder (chronic obstructive pulmonary disorder, asthma)	47 (17.7)
Mood disorder (depression, bipolar disorder, anxiety disorder)	191 (71.8)
Prescribed medication for comorbid psychiatric condition	173 (65.0)

ICD-9: International Classification of Diseases, 9th Revision.

≤12 mg and 56.4% received ≥16 mg based on the last recorded prescription.

3.4. Substance abuse treatment outcomes

3.4.1. Retention on buprenorphine treatment. Of the 266 patients, 88.4% were maintained on BPN at 1 month, 71.8% at 3 months, and 56.8% at 6 months (Fig. 1). Of the 136 patients who had at least 1 year of observation, 61.6% were still on BMT at 12 months (data not shown).

In the adjusted analysis examining the likelihood of retention on BMT at 6 months (Table 3), the covariates found to be positively

Table 2

Types and frequency of healthcare utilization at health center while receiving buprenorphine maintenance therapy (N = 266).

Medical visits[a]	
Number of patients who had at least 1 medical visit (%)	241 (90.6)
Mean number of visits per month of BMT for those who had at least 1 medical visit (range)	1.7 (0.07–6.9)
Mean number of visits per month of BMT for the total cohort (range)	1.6 (0.0–6.9)
Behavioral health visits[a]	
Number of patients who had at least 1 behavioral health visit (%)	150 (56.3)
Mean number of visits per month of BMT for those who had at least 1 behavioral health visit (range)	1.6 (0.05–8.0)
Mean number of visits per month of BMT for the total cohort (range)	0.9 (0.0–8.0)
Substance Abuse Counseling visits[a]	
Number of patients who had at least 1 substance abuse counseling visit (%)	141 (53.0)
Mean number of visits per month of BMT for those who had at least 1 substance abuse counseling visit (range)	1.2 (0.05–4.3)
Mean number of visits per month of BMT for the total cohort (range)	0.6 (0.0–4.3)
All visits[a]	
Mean number of visits per month of BMT for the total cohort (range)	3.1 (0.5–8.3)

BMT: buprenorphine maintenance therapy.

[a] If individuals stayed in treatment for less than a month, the total number of visits was set to one month.
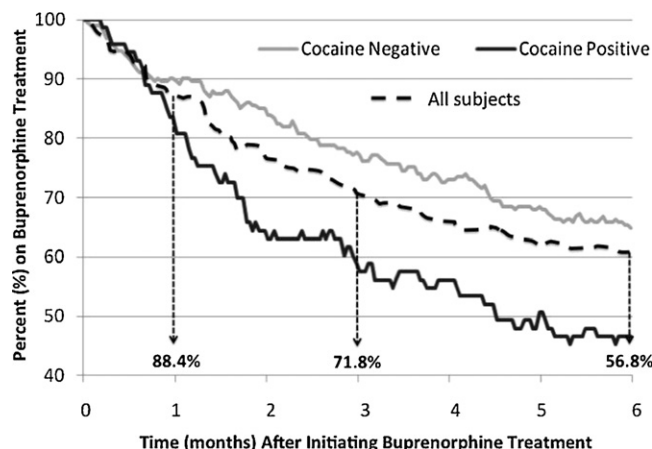

Fig. 1. Retention on buprenorphine maintenance therapy, overall and stratified by cocaine use (N = 266).

correlated were older age, female gender, HCV infection, receipt of psychiatric medication, and receipt of on-site substance abuse counseling; baseline cocaine use was negatively correlated with retention. In the adjusted analysis for 12-month retention on BMT, significant correlations persisted positively for receipt of psychiatric medication and receipt of on-site substance abuse counseling and negatively for baseline cocaine use.

Only about one third (32.7%) of the cohort persistently remained on BMT, receiving continuous BMT without any interruption in treatment. Therefore, about two thirds had non-persistent treatment, experiencing at least one BMT gap of 2 or more weeks during their observation period. Overall, 39.9% of subjects experienced one gap while 17.7% had 2 gaps, 5.6% had 3 gaps, and 4.1% had 4 or 5 gaps. For the 67.3% who experienced treatment gaps, the mean gap length was 116.4 days, ranging from 14 to 482 days.

3.4.2. Opioid-free time. The 266 subjects enrolled in the BMT program underwent, on average, 1.6 monthly urine toxicology screens ranging from 0 to 4 tests per month. Just under a third (29.7%) of patients had all urine samples that were collected during observation test negative for opioids and 41.0% had all their urines test negative for cocaine (Table 4). About a third (33.5%) of patients had a baseline urine screen test positive for opioids and 26.7% tested positive for cocaine. Of the 134 patients who were still on BMT at the end of observation, 24.4% had their last urine test positive for opioids and 14.2% for cocaine. When examining all urines sampled in the last month of observation, 72.4% of these patients tested negative for opioids, 81.3% tested negative for cocaine, and 66.4% tested negative for both. Of the 132 patients who were not on BMT at the end of observation, 51.0% had their last urine test positive for opioids and 40.0% for cocaine. Only 34.9% had all urines in the last month test negative for opioids, 47.0% test negative for cocaine and 20.5% test negative for both.

In the multivariate analyses examining covariates of opioid-free time (Tables 5a–5c), each of the three definitions were analyzed separately. In examining opioid-free urines in the last month of treatment, receipt of psychiatric medication was positively correlated and any cocaine use was negatively correlated. Similarly, in examining the proportion of all collected opioid-free urine screens, the only covariate that was positively correlated was receipt of psychiatric medication. Last, in examining duration of opioid-free time, having a mood disorder diagnosis was positively correlated while baseline cocaine use was negatively correlated.

Table 3
Covariates associated with non-retention on buprenorphine maintenance therapy.[a]

Covariates	6-Month non-retention N=266						12-Month non-retention N=136					
	Unadjusted HR			Adjusted HR			Unadjusted HR			Adjusted HR		
	H.R.	95% CI	P value	H.R.	95% CI	P value	H.R.	95% CI	P value	H.R.	95% CI	P value
Age	0.96	(0.94, 0.98)	<0.01	0.96	(0.94, 0.98)	<0.01	0.99	(0.96, 1.02)	0.62			
Gender												
Male	Ref			Ref								
Female	0.76	(0.49, 1.1)	0.19	0.59	(0.37, 0.92)	0.02	0.69	(0.36, 1.3)	0.26			
Site												
Site 1	Ref											
Site 2	0.80	(0.54, 1.20)	0.22				0.78	(0.45, 1.4)	0.39			
Prescriber specialty												
Psychiatry	Ref											
Primary care	0.85	(0.79, 1.72)	0.45				0.67	(0.85, 2.59)	0.16	[b]		
Baseline cocaine screen												
Negative	Ref			Ref			Ref			Ref		
Positive	1.73	(1.18, 2.54)	0.01	2.18	(1.35, 3.50)	<0.01	2.06	(1.20, 3.51)	<0.01	3.12	(1.57, 6.16)	<0.01
Any cocaine screen												
Negative	Ref						Ref					
Positive	1.36	(0.94, 1.97)	0.10	[b]			1.22	(0.73, 2.04)	0.44			
Mood disorder												
No	Ref						Ref					
Yes	1.06	(0.81, 1.40)	0.65				1.08	(0.73, 1.59)	0.68			
Prescribed psychiatric medication												
No	Ref			Ref			Ref			Ref		
Yes	0.57	(1.2, 2.6)	<0.01	0.69	(0.47, 1.01)	0.05	0.41	(0.24, 0.69)	<0.01	0.36	(0.20, 0.62)	<0.01
HIV-infected												
No	Ref						Ref					
Yes	1.16	(0.56, 1.8)	0.98				1.39	(0.66, 2.94)	0.38			
HCV-infected												
No	Ref			Ref			Ref					
Yes	0.74	(0.52, 1.10)	0.13	0.56	(0.36, 0.86)	0.01	0.95	(0.56, 1.60)	0.85			
Receipt of on-site substance abuse counseling												
No	Ref			Ref			Ref			Ref		
Yes	0.55	(0.37, 0.78)	<0.01	0.54	(0.36, 0.79)	<0.01	0.39	(0.22, 0.67)	<0.01	0.34	(0.19, 0.59)	<0.01
AIC goodness of fit					1169.28						502.9	

AIC = Akaike Information Criterion; Ref = referent.

[a] Estimates from a Cox Proportional Hazard model.

[b] Non-significant variables were excluded based on AIC in the multivariate model.

4. Discussion

4.1. Substance abuse treatment outcomes

The results confirm that BMT retention in a FQHC, a real-world clinical setting, is similar to results observed in other settings as varied as specialty substance abuse clinics, HIV clinics, academic centers, and hospitals and where patients with complex medical and psychiatric comorbidity were excluded. Of note, just above half of our cohort received daily buprenorphine dosing of ≥ 16 mg. Given a recent meta-analysis which determined that daily doses of 16–32 mg predicted better retention than lower doses, the implication that even better retention rates could be achieved if higher dosages of buprenorphine are prescribed is intriguing and merits further investigation (Fareed et al., 2012).

Two factors were found to be significantly associated with improved retention on buprenorphine at both 6 and 12 months: receiving on-site substance abuse counseling and receiving

Table 4
Urine toxicology screening results of 266 opioid-dependent patients on buprenorphine maintenance therapy.

Number of urine screens done per person per month of BMT, mean (range)		1.6 (0.0–4.1)	
Percent of patients with all urines collected testing negative for opioids (95% CI)		29.7 (24.1–35.2)	
Percent of patients with all urines collected testing negative for cocaine (95% CI)		41.0 (35.7–46.4)	
Percent of baseline urine screens positive for opioids (95% CI)		33.5 (27.0–39.0)	
Percent of baseline urine screens positive for cocaine (95% CI)		26.7 (21.0–32.0)	
	Patients still on BMT at end of observation period (N=134)	Patients not on BMT at end of observation period (N=132)	P value
Last urine screen positive for opioids, % (95% CI)	24.4 (17.0–32.0)	51.0 (41.0–60.0)	<0.01
Last urine screen positive for cocaine, % (n)	14.2 (19)	40.0 (53)	<0.01
Urine screens negative for opioids in last month of treatment or observation, % (n)	72.4 (97)	34.9 (46)	<0.01
Urine screens negative for cocaine in last month of treatment or observation, % (n)	81.3 (109)	47.0 (62)	<0.01
Urine screens negative for both opioids and cocaine in last month of treatment or observation, % (n)	66.4 (89)	20.5 (27)	<0.01

BMT: buprenorphine maintenance therapy.

Table 5a
Covariates associated with opioid-free time, defined as lack of opioids in the urine in the last month of observed treatment.

Covariates	Opioid negative urine samples in last month of BMT					
	Univariate analysis			Multivariate analysis		
	Logistic regression			Logistic regression		
	OR	95% CI	P value	AOR	95% CI	P value
Age	1.01	(0.98, 1.03)	0.46			
Gender						
Male	Ref					
Female	1.21	(0.70, 2.07)	0.49			
Site						
Site 1	Ref					
Site 2	0.98	(0.59, 1.60)	0.94			
Specialty						
Psychiatry	Ref					
Primary care provider	**0.64**	**(0.36, 1.10)**	**0.11**	[a]		
Baseline cocaine screen						
Negative	Ref					
Positive	**0.52**	**(0.29, 0.92)**	**0.03**	[a]		
Any cocaine screen						
Negative	Ref			Ref		
Positive	**0.43**	**(0.25, 0.72)**	**<0.01**	**0.43**	**(0.25, 0.73)**	**<0.01**
Receipt of on-site substance abuse counseling						
No	Ref					
Yes	**0.68**	**(0.41, 1.11)**	**0.13**	[a]		
Mood disorder						
No	Ref					
Yes	**1.56**	**(0.88, 2.73)**	**0.12**	[a]		
Prescribed psychiatric medication						
No	Ref			Ref		
Yes	**1.67**	**(0.98, 2.83)**	**0.06**	**1.66**	**(1.03, 2.85)**	**<0.01**
HIV-infected						
No	Ref					
Yes	0.87	(0.38, 1.98)	0.75			
HCV-infected						
No	Ref					
Yes	0.87	(0.52, 1.45)	0.60			
AIC goodness of fit				356		

BMT = buprenorphine maintenance therapy; Ref = referent; AIC = Akaike Information Criterion; GLM = generalized linear model; OLS = ordinary least square regression.

[a] Non-significant variables were excluded by AIC/criteria in the multivariate model.

psychiatric medication. Baseline cocaine use, however, was associated with poorer retention. The findings that on-site provision of counseling services improves retention are consistent with models that are either co-located or fully integrated (Basu et al., 2006; Sylla et al., 2007; Weiss et al., 2011). Furthermore, subjects prescribed psychiatric medications had improved retention also suggests that concomitant treatment of mental illness may be critical for BMT retention. Similar to other studies, cocaine use was associated with decreased retention (Sullivan et al., 2011). Indeed, non-cocaine users had higher BMT retention noted as early as 1 month after initiation (Fig. 1). Early detection of cocaine should alert providers early into treatment and encourage concentration of resources to help retain patients in BMT, perhaps through counseling intensification (Copenhaver et al., 2007).

Last, being older, female, and HCV-infected were each associated with improved retention at 6 months though the association was not maintained at 12 months. A larger and longer study may be needed to better elucidate the association between these covariates and retention.

Opioid-free time, on the other hand, is not comparable across studies given the varied manner in which this variable has previously been defined and measured. Nevertheless, just under a third of patients were persistently opioid-free throughout the study and a similar proportion tested positive for opioids at baseline. As expected, however, opioid use decreased with improved BMT retention. Compared to those who discontinued BMT, those who were retained were significantly more likely to have negative terminal urine screens for both opioids and cocaine. Moreover, two

factors associated with increased BMT retention were also associated with opioid-free time, including treatment for a mood disorder and not using cocaine.

These findings have broader implications globally. While countries in Western Europe, in particular France, have been prescribing BMT in primary care settings since 1996, other countries where BMT is more highly regulated (Bruce et al., 2007; Carrieri et al., 2006) can be assured that they can achieve good retention and reduce opioid use in real-world settings. Such findings are likely to have important health improvements where opioids contribute to negative health consequences (Altice et al., 2010).

In summary, improved treatment outcomes associated with substance abuse counseling and with screening for and treating mood disorders underscore the importance of integrating mental health screening and care into primary care-based BMT. The negative impact of cocaine use on study outcomes and lack of pharmacologica therapy for treating cocaine addiction underscores the need for alternative strategies to facilitate reductions or cessation in cocaine use among BMT patients, including cocaine-specific behavioral therapies (Penberthy et al., 2010; Petry et al., 2012). Given the constrained resources of FQHCs, however, these patients may need referrals to specialized community-based treatment programs. Such strategies may clinically improve BMT retention, increase opioid-free time, and continuously engage this vulnerable population in care at FQHCs. Moreover, the finding that two-thirds had at least one 2-week gap in treatment lasting on average 4 months underscores treatment non-persistence and re-entry into care in real-world settings. Such findings should

Table 5b
Covariates associated with opioid-free time, defined as the percentage of all collected urines free of opioids.

Covariates	Proportion of all urine samples collected that were negative for opioids					
	Univariate analysis			Multivariate analysis		
	GLM regression			GLM regression		
	OR	95% CI	P value	AOR	95% CI	P value
Age	1.00	(0.96, 1.02)	0.74			
Gender						
Male	Ref					
Female	**1.72**	**(0.94, 3.14)**	**0.08**	[a]		
Site						
Site 1	Ref					
Site 2	0.94	(0.54, 1.60)	0.82			
Specialty						
Psychiatry	Ref			Ref		
Primary care provider	**0.57**	**(0.30, 1.04)**	**0.07**	0.59	(0.32, 1.10)	0.10
Baseline cocaine screen						
Negative	Ref					
Positive	0.73	(0.40, 1.31)	0.30			
Any cocaine screen						
Negative	Ref					
Positive	0.71	(0.40, 1.22)	0.22			
Receipt of on-site substance abuse counseling						
Mood disorder						
No	Ref					
Yes	0.94	(0.55, 1.59)	0.82			
No	Ref					
Yes	**1.86**	**(1.04, 3.31)**	**0.03**	[a]		
Prescribed psychiatric medication						
No	Ref			Ref		
Yes	**1.89**	**(1.08, 3.27)**	**0.02**	**1.83**	**(1.05, 3.18)**	**0.03**
HIV-infected						
No	Ref					
Yes	1.11	(0.46, 2.69)	0.81			
HCV-infected						
No	Ref					
Yes	0.98	(0.57, 1.69)	0.96			
AIC goodness of fit				102		

BMT = buprenorphine maintenance therapy; Ref = referent; AIC = Akaike Information Criterion; GLM = generalized linear model; OLS = ordinary least square regression.

[a] Non-significant variables were excluded by AIC/criteria in the multivariate model.

inform clinical providers and researchers designing future clinical trials.

In addition, most (80.5%) patients initiated care at the FQHC specifically seeking BMT. This suggests that patients in communities where FQHCs provide BMT would indeed enter primary care and have the potential to also receive routine screening and treatment for a multitude of other comorbid conditions. Furthermore, no differences in treatment outcomes were noted between family practice and specialty psychiatry prescribers. All these findings underscore the value and need of integrating BMT programs into FQHCs to improve the likelihood that they can truly fulfill their role as patient-centered medical homes (PCMH) by addressing substance abuse treatment.

4.2. Limitations of study

This study was observational and retrospective with no controls and therefore lacks the rigor of a randomized controlled trial (RCT) in determining causal factors associated with the treatment outcomes examined. It does represent, however, a rigorous analysis using implementation science methodologies that provide important insight into expanding an evidence-based intervention, BMT, into a diverse clinical setting. Furthermore, given the sample size of 266 patients, associations could be identified between retention in BMT and opioid-free time, and the correlates examined for each. Prospective RCTs are needed to better differentiate the benefits of BMT in these settings, yet real-world implementation science studies are critical to examine how idealized RCTs are translated in community settings.

The retrospective chart review limited the types and content of data collected to what providers recorded in charts during the course of real-world clinic visits. Therefore, additional data such as incarceration history, type of opioids used, route of drug use, attendance at off-site addiction counseling sessions, and reasons for treatment termination (e.g., relapse, transfer to methadone, or transfer to higher level of care), were not available. Given this limitation, we were unable to compare those subjects who were enrolled in counseling on-site with those who may have received counseling off-site. The strong association we found between on-site counseling and BMT retention, however, still indicates that integrating counseling on-site, as espoused by the PCMH model, is worthwhile to promote successful treatment. Moreover, the availability of EHR for chart review provided easy, systematic and complete extraction of real-world information such as visits, urine toxicology results, laboratory results, and problem lists. While data collection errors may still occur despite EHR access, we limited errors through double data collection techniques.

Though a statewide FQHC network was examined, data should be interpreted with caution due to the network being within one state and may not apply to FQHCs elsewhere. Nevertheless, the sites within the FQHC differed in number, training, specialty services and experience of staff involved directly and indirectly in the BMT program.

Furthermore, the FQHC BMT protocol is flexible and allows for differences in prescriber practice style and available resources.

Table 5c
Covariates associated with opioid-free time, defined as the duration of opioid-free time while on prescribed buprenorphine.

Covariates	Proportion of all urine samples collected that were negative for opioids × [duration of BMT – gap times] (duration of opioid-free time)					
	Univariate analysis			Multivariate analysis		
	OLS			OLS		
	Beta	95% CI	P value	Beta	95% CI	P value
Age	**2.44**	**(0.04, 4.82)**	**0.05**	2.08	(−0.29, 4.44)	0.09
Gender						
Male	Ref					
Female	28.36	(−19.0, 75.8)	0.24			
Site						
Site 1	Ref					
Site 2	16.58	(−28.1, 61.2)	0.47			
Specialty						
Psychiatry	Ref					
Primary care provider	27.37	(−20.0, 75.3)	0.26			
Baseline cocaine screen						
Negative	Ref			Ref		
Positive	**−50.05**	**(−102, 2.05)**	**0.06**	**−50.42**	**(−99.1, −0.36)**	**<0.05**
Any cocaine screen						
Negative	Ref					
Positive	**−41.60**	**(−86.1, 3.52)**	**0.07**	[a]		
Receipt of on-site substance abuse counseling						
No	Ref			Ref		
Yes	**44.65**	**(0.90, 88.3)**	**0.05**	39.87	(−3.55, 83.3)	0.07
Mood disorder						
No	Ref			Ref		
Yes	**72.00**	**(23.8, 120)**	**<0.01**	**65.9**	**(18.23, 113.6)**	**<0.01**
Prescribed psychiatric medication						
No	Ref			Ref		
Yes	**62.72**	**(17.2, 108)**	**0.01**	[a]		
HIV-infected						
No	Ref					
Yes	−11.04	(−39.0, 17.8)	0.45			
HCV-infected						
No	Ref					
Yes	−0.35	(−18.2, 17.9)	0.97			
AIC goodness of fit				3512.2		

BMT = buprenorphine maintenance therapy; Ref = referent; AIC = Akaike Information Criterion; GLM = generalized linear model; OLS = ordinary least square regression.

[a] Non-significant variables were excluded by AIC/criteria in the multivariate model.

Frequency of patient visits, number of urine toxicology screens performed, thresholds for terminating BMT and for recommending higher levels of care, and insistence of patient participation in on-site or off-site substance abuse counseling are all dependent upon individual providers and thus variable. This variability, however, represents real-world practice and hence these results more accurately represent real-world outcomes. This study involved three primary care providers but only one psychiatrist, which may limit the value of the comparison of results between primary and specialty care services. The psychiatrist, however, was the most experienced BMT provider and thus could indeed potentially serve as the internal standard to which others could be compared.

We believe these study findings can greatly inform FQHCs across the nation to strive toward healthcare integration within PCMHs by providing BMT to their opioid dependent patients. Moreover, identifying correlates of treatment success as defined by retention in care and opioid-free time could influence the design of other BMT programs. Factors proven to be associated with improved outcomes could determine what resources are needed to deliver effective quality care to opioid dependent patients. Such factors could also help direct the allocation of resources within a program by identifying, for instance, the type of patient that may need extra resources at the outset of treatment.

The implications of expanding BMT to FQHCs could be significant not only to individuals but on a societal, economic, and public health level. Decreasing opioid dependence in communities and engaging these patients in primary care could result in increased health promotion and disease prevention and care, reduced emergency department visits (Schwarz et al., 2012), decreased opioid-related medical complications, including overdoses, abscesses, endocarditis, osteomyelitis, HIV and HCV transmission, and increased societal benefits including decreased healthcare costs, decreased crime, increased family cohesion, and increased employment. Expanding access to BMT for opioid-dependent persons has the great potential to provide considerable public health benefits (Krantz and Mehler, 2004).

Contributors

All authors participated in the research and manuscript preparation and have approved the final manuscript. The authors contributed to the other components of the paper: Haddad and Altice reviewed the literature, Zelenev and Altice contributed to the statistical analysis and Haddad prepared the first draft of manuscript, while Haddad and Zelenev contributed to the data management and the study design was done by Haddad, Zelenev and Altice.

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